# Fosamprenavir (FPV, Lexiva)

For additional information see Drugs@FDA:
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

## Formulations

**Tablets:** 700 mg FPV calcium

**Oral suspension:** 50 mg/mL

## Dosing Recommendations

**Neonate/infant dose:**
Not approved for use in neonates/infants.

**Pediatric dose (2–18 years of age):**
Dosing regimen depends on whether patient is antiretroviral (ARV) naive or ARV experienced. Once-daily dosing is not recommended for pediatric patients.

***ARV-naive patients (2–5 years of age):***
*Unboosted (without ritonavir [RTV]):*
FPV 30 mg/kg (maximum dose 1,400 mg) twice daily.

***ARV-naive patients (>6–18 years of age):***
*Unboosted (without RTV):*
FPV 30 mg/kg (maximum dose 1,400 mg) twice daily.

***or***

*Boosted with RTV:*
FPV 18 mg/kg (maximum dose 700 mg) +
RTV 3 mg/kg (maximum dose 100 mg), both twice daily.

***ARV-experienced patients (>6–18 years of age):***
*Boosted with RTV:*
FPV 18 mg/kg (maximum dose 700 mg) + RTV 3 mg/kg (maximum dose 100 mg), both twice daily.

*Note:* When administered without RTV, the adult regimen of FPV tablets (FPV 1,400 mg twice daily) can be used for patients weighing ≥47 kg ***or*** when administered with RTV, the adult regimen of 700 mg FPV tablets + 100 mg RTV, both given twice daily, can be used in patients weighing ≥39 kg. RTV pills can be used in patients weighing ≥33 kg.

**Adolescent (>18 years of age)/adult dose:**
Dosing regimen depends on whether the patient is ARV naive or ARV experienced.

## Selected Adverse Events

- Diarrhea, nausea, vomiting
- Skin rash (FPV has a sulfonamide moiety. Stevens-Johnson syndrome [SJS] and erythema multiforme have been reported.)
- Headache
- Hyperlipidemia, hyperglycemia
- Nephrolithiasis
- Transaminase elevation
- Fat maldistribution
- Possible increased bleeding episodes in patients with hemophilia

## Special Instructions

- FPV tablets with RTV should be taken with food. FPV tablets without RTV can be taken with or without food. Pediatric patients should take the suspension with food.
- Patients taking antacids or buffered formulations of didanosine (ddI) should take FPV at least 1 hour before or after antacid or ddI use.
- FPV contains a sulfonamide moiety. The potential for cross sensitivity between FPV and other drugs in the sulfonamide class is unknown. FPV should be used with caution in patients with sulfonamide allergy.
- Shake FPV oral suspension well prior to use. Refrigeration is not required.

## Metabolism

- The prodrug FPV is rapidly and almost completely hydrolyzed to amprenavir (APV) by cellular phosphatases in the gut as FPV is absorbed.

***ARV-naive patients:***
*Unboosted (without RTV), twice-daily regimen:*
FPV 1,400 mg twice daily.
*Boosted with RTV, twice-daily regimen:*
FPV 700 mg + RTV 100 mg, both twice daily.
*Boosted with RTV, once-daily regimen:*
FPV 1,400 mg + RTV 100–200 mg, both once daily.

***Protease inhibitor (PI)-experienced patients:***
FPV 700 mg + RTV 100 mg, both twice daily.

Once-daily administration of FPV + RTV is not recommended in PI-experienced patients.

***FPV in combination with efavirenz (EFV) (adults):***
Only FPV boosted with RTV should be used in combination with EFV.

*Twice-daily regimen:*
FPV 700 mg + RTV 100 mg, both twice daily + EFV 600 mg once daily.

*PI-naive patients only, once-daily regimen:*
FPV 1,400 mg + RTV 300 mg + EFV 600 mg, all once daily.

***FPV in combination with maraviroc (MVC) (adults):***
See MVC section for dosing of FPV with MVC.

- APV is a cytochrome P450 3A4 (CYP3A4) inhibitor, inducer, and substrate.
- ***Dosing in patients with hepatic impairment:*** Dosage adjustment is recommended.

***Drug Interactions*** (See also the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.):

- Fosamprenavir has the potential for multiple drug interactions.
- Before fosamprenavir is administered, the patient's medication profile should be carefully reviewed for potential drug interactions with fosamprenavir.

***Major Toxicities:***

- *More common:* Vomiting, nausea, diarrhea, perioral paresthesias, headache, rash, and lipid abnormalities.
- *Less common (more severe):* Life-threatening rash, including SJS, in <1% of patients. Fat maldistribution, neutropenia, and elevated serum creatinine kinase levels.
- *Rare:* New onset diabetes mellitus, hyperglycemia, ketoacidosis, exacerbation of pre-existing diabetes mellitus, spontaneous bleeding in hemophiliacs, hemolytic anemia, elevation in serum transaminases, angioedema, and nephrolithiasis.
- *Pediatric specific:* In clinical trials of fosamprenavir, vomiting was more frequent in pediatric patients (30%–56%) than in adult patients (10%–16%)[1].

***Resistance:*** The International Antiviral Society-USA (IAS-USA) maintains a list of updated resistance mutations (see http://www.iasusa.org/resistance_mutations/index.html) and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation (see http://hivdb.stanford.edu/pages/GRIP/APV_FPV.html).

***Pediatric Use:*** Fosamprenavir is Food and Drug Administration (FDA) approved for use in children as young as 2 years of age.

Fosamprenavir was studied in two open-label trials in both treatment-experienced and treatment-naive pediatric patients 2–18 years of age[2-3]. In one study, twice-daily dosing regimens (with or without ritonavir) were evaluated in combination with other ARV agents[3]. Overall, fosamprenavir was well tolerated and effective in suppressing viral load and increasing CD4 cell count. In the second trial, once-daily fosamprenavir/ritonavir was studied[2]. Following information about suboptimal response to once-daily dosing in treatment-experienced adults, pediatric patients were allowed to switch to twice-daily therapy; however, few patients (10 of 69) opted to switch to twice-daily therapy (median time to switch: 45 weeks). At 24 and 48 weeks of therapy, HIV RNA was <400 copies/mL in 66% and 47% among PI-naive subjects, respectively, and 57% and 43% among PI-experienced subjects, respectively. These data were insufficient to support a once-daily dosing regimen of ritonavir-boosted fosamprenavir in children; therefore, once-daily dosing is not recommended for pediatric patients.

## References


1. Food and Drug Administration. Lexiva FDA Label. Accessed June 20, 2011. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021548s024,022116s008lbl.pdf. 2010.
2. Chadwick E, Borkowsky W, Fortuny C, et al. Safety and antiviral activity of fosamprenavir/ritonavir once daily regimens in HIV-infected pediatric subjects ages 2 to 18 years (48-week interim data, study apv20003). Paper presented at: 14th Conference on Retroviruses and Opportunistic Infections (CROI); February 25-28, 2007; Los Angeles, CA. Abstract 719.
3. Cunningham C, Freedman A, Read S, et al. Safety and antiviral activity of fosamprenavir-containing regmens in HIV-infected 2- to 18-year-old pediatric subjects (interim data, study apv29005). Paper presented at: 14th Conference on Retroviruses and Opportunistic Infections (CROI); February 25-28, 2007; Los Angeles, CA. Abstract 718.